REMARKS

Formal Matters

Claims 1, 5-7, 19-22, 24-29 and 31 are pending.

Claims 1, 5-7, 19-22, 24-29 and 31 were examined and rejected.

Claims 8-18 are canceled without prejudice.

Claims 1 and 22 are amended. The amendments to the claims were made solely in the interest of expediting prosecution, and are not to be construed as an acquiescence to any objection or rejection of any claim. Support for the amendments are found in the claims as originally filed, and throughout the specification, in particularly at the following exemplary locations: page 11, line 8. Accordingly, no new matter is added.

Applicants respectfully request reconsideration of the application in view of the remarks made herein.

Sequence compliance

The Office Action states that the application fails to comply with the requirements of 37 C.F.R. § 1.821-1.825 because the sequences set forth in Figures 1A-1C are not properly identified.

The section entitled "Brief Description of the Accompanying Figure", as found on page 6 of this patent application, has been amended to recite SEQ ID NOS: 1 and 2. Accordingly, the sequences provided in Figures 1A-1C are now properly identified. The sequences in Figures 1A-1C are not new, thus no substitute sequence listing is necessary. The Applicants respectfully submit that this application now meets the requirement of 37 C.F.R. § 1.821-1.825.

Withdrawal of this objection is respectfully requested.

Rejection under 35 U.S.C. § 101 - Utility

Claims 1, 5-7, 19-22, 24-29 and 31 stand rejected under 35 U.S.C. § 101 on the grounds that the claimed invention has no apparent or disclosed specific and substantial credible utility. This rejection is again traversed.

The Utility Examination Guidelines (Federal Register 66, No. 4, January 5, 2001; hereinafter "The Guidelines") provides instructions for examining patent applications for compliance with the utility requirement of 35 U.S.C. § 101.

The Guidelines state:

> "(a) ***If the applicant has asserted that the claimed invention is useful for any practical purpose*** (i.e., it has a "specific and substantial utility") ***and the assertion would be considered credible*** by a person of ordinary skill in the art, ***do not impose a rejection based on lack of utility***." (p. 1098, col. 1).

Furthermore,

> "Office personnel ***must*** accept an opinion from a qualified expert that is based upon relevant facts whose accuracy is not being questioned; ***it is improper to disregard the opinion*** solely because of a disagreement over the significance or meaning of the facts offered". (p. 1099, col. 1).

Accordingly, if a utility is asserted in a patent application and that utility would be considered credible one of skill in the art (termed herein a "skilled person"), the claims must have patentable utility. Further, if an opinion of an expert is offered, e.g., by means of an Declaration under C.F.R. § 1.132, it cannot simply be ignored because it is contrary to the Office's position.

The instant specification states that "detection of the encoded protein should provide a useful tumour marker and/or prognostic indicator" on page 1, lines 4-5. Since a "tumor marker" finds use as a diagnostic for cancerous cells, the Applicants respectfully submit that the claimed subject matter may be used as a cancer diagnostic. This utility is unambiguously asserted in the instant patent application, and, in view of the factual evidence entered into the record by the Applicants is not incredible.

The asserted utility of the claimed subject matter is supported by, for example, a) post-filing publications (e.g., Monz et al, Clin Cancer Res. 7:113-9, 2001), demonstrating that the claimed sequence is overexpressed in meningiomas), and b) gene expression data provided by Dr. Hitoshi in his declaration. No more is required by the law to satisfy the utility requirement of 35 U.S.C. § 101, and this

rejection should be withdrawn without any further discussion. Why does the Office think that this asserted utility is incredible in view of this factual evidence?

The Office has spent considerable effort in trying to support a conclusion that the claimed polynucleotide cannot be used as a tumor indicator. However, the Office's sole evidence to supports its case is that the instant specification provides no "evidence or sound scientific reasoning" (e.g., data) to support the claimed subject matter's utility as a tumor indicator.[1] However, the Applicants note that there is no such requirement in the MPEP, The Guidelines, or the law that requires "evidence or sound scientific reasoning" to be in a patent application to support an asserted utility. According to The Guidelines, all that is required to meet the utility requirement of 35 U.S.C. § 101 is a credible, specific and substantial utility – nowhere does it state that the utility must be evidenced or supported by "sound scientific reasoning" in the specification as filed. Accordingly, the Applicants respectfully submit that this rejection finds no basis in current law, and, accordingly, this rejection should be withdrawn. The Applicants respectfully request that if this rejection is to be maintained, the Office sets forth, for the record, its reasoning to require a showing of "evidence" in a patent application to support an asserted utility – an asserted utility, as long as it is credible, should be sufficient. If the Office cannot show such requirement, then it should withdraw the rejection.

Furthermore, the data of Dr. Hitoshi's Declaration shows, without a shadow of a doubt, that the claimed subject matter may be used to detect cancerous cells. So much is acknowledged in the Office Action.[2] The fact that Dr. Hitoshi's data was not included in the patent application is of no matter: the asserted utility remains the same, whether or not it is included. It also appears that the data introduced by Dr. Hitoshi's Declaration is being ignored by the Office solely on the grounds that it is produced subsequent to the filing date of the instant application and not included in the application.[3]

In addition, the Declaration of Dr. Histoshi did more than provide data that supports the asserted utility of the instant application. Dr. Histoshi also reviewed the application, and pointed to specific

---

[1] See, e.g., page 5 "The instant specification fails to provide any evidence or sound scientific reasoning to allow a conclusion.....", and "there is no disclosure that the claimed polynucleotides are expressed in altered levels or forms in any specific, diseased tissue.....", etc.

[2] See page 6, "additional data show that 2.2412 was expressed at significantly higher levels in two types of lung cancer and three types of breast cancer".

[3] See, e.g., page 7, "Any further subsequent characterization of the claimed DNA and encoded protein, ...is considered to part of the act of invention.", "the instant specification, as filed, fails to provide any information regarding using novel 2.2412 sequences as specific markers for breast and lung cancer", and "there is no evidence of record in the instant specification, which specifically associates the instant DNA or encoded protein with any human cancers".

statements in the application that provide a credible association of 2.2412 expression and human cancers.[4] Specifically, Dr. Hitoshi declares:

> 7. The '196 application sets out the following statements (page and line numbers in brackets refer to the specific parts of the '196 application::
>
> a) **2.2412 protein is an effector protein for the Grb7 family of signalling proteins** (a protein that specifically binds to a signaling protein to facilitate a signal transduction cascade)
>
> i) **2.2412 protein specifically binds Grb14 and specifically binds Grb7** (page 10, line 26 to page 11, line 32)
>
> ii) **binding of 2.2412 protein to Grb14 requires the N-terminal region of Grb14, which contains highly conserved proline-rich motif thought to mediates interaction of the Grb7 family of proteins with their effectors** (page 11, lines 29-32)
>
> iii) **2.2412 contains multiple ankyrin repeats, which are known to have a role in protein-protein interactions** (page 9, lines 25-34)
>
> b) **Grb7 family members are signal transduction molecules that exhibit differential expression in certain human cancers (particularly breast cancer)** (page 5, lines 13-15). Specifically, at the time of filing
>
> i) Grb7 family members were known to be associated with oesophageal carcinoma,[1] primary gastric cancer,[2] and breast cancer.[3]
>
> ii) **Grb14 was known to be differentially expressed in breast cancer**[4]
>
> iii) **Grb7 was known to be differentially expressed in breast cancer**[5]
>
> 8. Given that 2.2412 specifically binds Grb14 and specifically binds Grb7, each which were known at the time the application was filed (September23, 1997) to be differentially expressed in cancer cells compared to normal cells, it is reasonable to conclude that effectors for these proteins such as 2.2412 will also be differentially expressed (specification page 5, lines 13-16).
>
> (citations omitted)

---

[4] Declaration of Yasumichi Hitoshi Under 37 C.F.R. §1.132, paragraph 9.

Dr. Hitoshi reaches the conclusion that it is reasonable to conclude that the 2.2412 protein is differentially expressed in cancer cells based on analysis of statements in the specification relating to the interaction of 2.2412 protein with Grb7 and Grb14. **Dr. Hitoshi's conclusion that 2.2412 protein is differentially expressed in cancer is *independent of* and, in fact, *in spite of*, any of the statements to which the Office has repeatedly pointed as undermining the assertions of utility in the instant application**. The Office is reminded that, under both case law and its own rules of practice, the Office is required to consider the factual evidence in the record, including the Hitoshi Declaration and its factual underpinnings, and either accept them as true or rebut them with a factual showing of its own.[5] Applicants request that such a factual showing be provided in an affidavit by the Examiner under 37 C.F.R. § 1.104(d)(2).

Finally, with specific reference to the use of Declarations in response to rejections based on lack of utility, the Office is advised to review pages 17 of the Revised Interim Utility Guidelines Training Materials, as posted to the world wide website of the U.S.P.T.O at http://www.uspto.gov/web/offices/pac/utility/utilityguide. This example sets forth a hypothetical scenario with a fact pattern that is almost identical to the instant fact pattern. In the Example, a utility was asserted in a patent specification, the claims were rejected because the Examiner believed the utility to be incredible, an expert Declaration was filed under C.F.R. § 1.132 to support the asserted utility, and the rejection was ***withdrawn***. In view of these Training Materials and Dr. Hitoshi's declaration, this rejection should be withdrawn without any further discussion.

Accordingly, in view of the foregoing arguments, this rejection may be withdrawn.

Rejection under 35 U.S.C. § 112 - Written Description

Claims 1, 5-7, 20, 22-28 and 30 were rejected as containing subject matter which was not described in the specification in such a way as to reasonably convey to the skilled artisan that the inventors had, when the application was filed, possession of the claimed invention. This rejection is respectfully traversed as applied and as it maybe applied to the pending claims.

---

[5] *In re Alton*, 76 F.3d 1168, 1175, 37 U.S.P.Q.2d (BNA) 1578, 1583 (Fed. Cir. 1996).

Without wishing to acquiesce to the correctness of this rejection, the claims have been amended to encompass only those polynucleotide molecules that encode a polypeptide that binds Grb7. Accordingly, the claimed polynucleotides encode a biological activity.

This rejection is based on the assertion that "instant specification fails to describe the ***entire genus of polynucleotides*** which are encompassed by the claims" (emphasis added). In other words, the Office rejects the instant claims because they read on polynucleotide species that are not specifically described in the instant specification.

However, the fact that a claim may *read on* a species that is not specifically described in the claim is not a barrier to patentability of the claim. It is well established that even in an "unpredictable art," applicants "are *not* required to disclose *every* species encompassed by their claims . . . ."[6] Thus, features that apply to only some species within a generic claim – but not to *all* species encompassed by the claim – need not be described to satisfy the written description requirement. Otherwise, to claim a genus, every species within a genus would have to be explicitly described. That is not the law.[7]

In contrast to the Office's position, the guidance set forth in the "Synopsis of Application of Written Description Guidelines", as published to the world wide website of the U.S.P.T.O. on March 1st, 2000 (http://www.uspto.gov/web/offices/pac/writtendesc.pdf), indicates that the claims are adequately described.

Example 14 of the Synopsis describes a scenario that is very similar to that currently under examination. Example 14 provides an example of a specification that discloses the sequence of a polypeptide having the sequence of SEQ ID NO:3, and also discloses that the polypeptide has a certain activity. This example also states that the specification also "contemplates but does not exemplify" variants of SEQ ID NO:3, and provides an assay for measuring the activity of the protein. In this example, the claims are directed to polypeptides having a sequence that is at least 95% identical to that of SEQ ID NO: 3 and catalyze the reaction of A→B.

The Synopsis states that the claimed subject matter is adequately described by the specification and the requirements of 35 USC §112 first paragraph have been met because "The single species

---

[6] *In re Angstadt*, 537 F.2d 498, 502-03, 190 U.S.P.Q. (BNA) 214, 218, (C.C.P.A. 1976).

[7] *See Engel Indus., Inc. v. Lockformer Co.*, 946 F.2d 1528, 1531, 20 U.S.P.Q.2d (BNA) 1300, 1302 (Fed. Cir. 1991) ("Unclaimed subject matter is not subject to the disclosure requirements of § 112; the reasons are pragmatic: the disclosure would be boundless, and the pitfalls endless."). *See also Phillips Petroleum v. U.S. Steel Corp.*, 673 F. Supp. 1278, 1292, 6 U.S.P.Q.2d (BNA) 1065, 1074 (D. Del. 1987) ("The applicant is not required to include in his application support for matters not set forth in the claim."), *aff'd* 865 F.2d 1247, 9 U.S.P.Q.2d (BNA) 1461 (Fed. Cir. 1989).

disclosed is representative of the genus because all members have at least 95% structural identity with the reference compound and because of the presence of an assay which applicant provided for identifying all of the at least 95% identical variants of SEQ ID NO: 3 which are capable of the specified catalytic activity."

For the Examiner's convenience, Example 14 of the Synopsis of Application of Written Description Guidelines is reproduced below:

Example 14: Product by Function

Specification: The specification exemplifies a protein isolated from liver that catalyzes the reaction of **A B.** The isolated protein was sequenced and was determined to have the sequence as set forth in SEQ ID NO: 3. The specification also contemplates but does not exemplify variants of the protein wherein the variant can have any or all of the following: substitutions, deletions, insertions and additions. The specification indicates that procedures for making proteins with substitutions, deletions, insertions and additions is routine in the art and provides an assay for detecting the catalytic activity of the protein.

Claim:
A protein having SEQ ID NO: 3 and variants thereof that are at least 95% identical to SEQ ID NO: 3 and catalyze the reaction of A B.

Analysis:
A review of the full content of the specification indicates that a protein having SEQ ID NO: 3 or variants having 95% identity to SEQ ID NO: 3 and having catalytic activity are essential to the operation of the claimed invention. The procedures for making variants of SEQ ID NO: 3 are conventional in the art and an assay is described which will identify other proteins having the claimed catalytic activity. Moreover, procedures for making variants of SEQ ID NO: 3 which have 95% identity to SEQ ID NO: 3 and retain its activity are conventional in the art.

A review of the claim indicates that variants of SEQ ID NO: 3 include but are not limited to those variants of SEQ ID NO: 3 with substitutions, deletions, insertions and additions; but all variants must possess the specified catalytic activity and must have at least 95% identity to the SEQ ID NO: 3.

Additionally, the claim is drawn to a protein which **comprises** SEQ ID NO: 3 or a variant thereof that has 95% identity to SEQ ID NO: 3. In other words, the protein claimed may be larger than SEQ ID NO: 3 or its variant with 95% identity to SEQ ID NO: 3. It should be noted that "having" is open language, equivalent to "comprising".

The claim has two different generic embodiments, the first being a protein which comprises SEQ ID NO: 3 and the second being variants of

SEQ ID NO: 3. There is a single species disclosed, that species being SEQ ID NO: 3.

A search of the prior art indicates that SEQ ID NO: 3 is novel and unobvious.

There is actual reduction to practice of the single disclosed species.

The specification indicates that the genus of proteins that must be variants of SEQ ID NO: 3 does not have substantial variation since all of the variants must possess the specified catalytic activity and must have at least 95% identity to the reference sequence, SEQ ID NO: 3. The single species disclosed is representative of the genus because all members have at least 95% structural identity with the reference compound and because of the presence of an assay which applicant provided for identifying all of the at least 95% identical variants of SEQ ID NO: 3 which are capable of the specified catalytic activity. One of skill in the art would conclude that applicant was in possession of the necessary common attributes possessed by the members of the genus.

Conclusion: The disclosure meets the requirements of 35 USC §112 first paragraph as providing adequate written description for the claimed invention.

The Applicants respectfully submit that the fact pattern of the example set forth above is very similar to the instant fact pattern. In other words, the instant specification a) describes the sequence of a full length polypeptide 2.2412 (SEQ ID NO:2); b) describes that 2.2412 has Grb7 binding activity, c) "contemplate but does not exemplify" variants of 2.2412, and d) provides detailed methods of how Grb7 binding activity can be assayed (see e.g., the two-hybrid methods described in pages 6 and 7 of the instant specification).

As such, by the reasoning set forth in the Example 14 of the Synopsis, the instant claims should be considered adequately described by the specification, meeting the requirements of 35 USC §112, first paragraph.

Withdrawal of this rejection is respectfully requested.

Conclusion

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number RICE-012.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: November 19, 2003

By: _____
Carol L. Francis
Registration No. 36,518

BOZICEVIC, FIELD & FRANCIS LLP
200 Middlefield Road, Suite 200
Menlo Park, CA 94025
Telephone: (650) 327-3400
Facsimile: (650) 327-3231

F:\DOCUMENT\RICE\012\Response to OA dated August 19, 2003.doc